

## Post-mortem diagnosis: evolving a team approach



The decline in autopsy rates in the past four decades in developed countries (to less than 5% in the USA<sup>1</sup>) has paralleled continued discrepancies between clinical and autopsy diagnoses of up to 20–30%.<sup>2,3</sup> The interconnected causes of low autopsy rates include absence of predictable funding, clinical overconfidence in diagnostic modalities, reluctance to request and undertake autopsies, decreased expertise in autopsy, a scarcity of auditable standards and mandated autopsy rates, and reluctance of families to consent to autopsy.<sup>1,4</sup> The need for mortality data based on accurate post-mortem diagnosis of disease and identification of cause of death has increased interest in minimally or less-invasive procedures to replace or augment conventional autopsy.<sup>5</sup> However, uncertainty about the accuracy of less-invasive diagnostic techniques for post mortems and about integration with conventional autopsy has raised concerns about whether reliable population-based determination of cause of death can be maintained.

In *The Lancet*, Sudhin Thayyil and colleagues<sup>6</sup> report on the first large, prospective, validation study of fetuses, infants, and children comparing post-mortem MRI with conventional autopsy and a uniquely defined minimally invasive autopsy. The MRI protocol, optimised to acquire non-contrast T1-weighted and T2-weighted images of the brain, spine, and body on a 1.5 Tesla magnet, needed about 90 min scan time in fetuses and 60 min in children, and used three-dimensional sequences for image reconstruction in different planes. The conventional autopsy complied with UK national guidelines, including in-situ, macroscopic, and histological assessment of the brain and internal organs, and ancillary assessments, consisting of clinical history; ante-mortem diagnostic studies; post-mortem plain-film radiography; external examination; placental histopathological examination for fetuses; and laboratory tests, including genetic, metabolic, and microbiological studies. The minimally invasive autopsy consisted of these common ancillary assessments and post-mortem MRI, with no post-mortem sampling of tissues or body fluids other than blood, and no histological assessments.

MRI alone versus conventional autopsy was concordant in 222 (55.5%, 95% CI 50.6–60.3) of 400 cases for identification of cause of death or major pathological change. By contrast, minimally invasive versus

conventional autopsy was concordant in 357 (89.3%, 85.8–91.9) cases. However, concordance varied substantially by age. A high concordance for fetuses (95–96%), and relatively high rates for newborn babies (81%) and infants (85%), contrasted with that of only 53.6% for children aged between 12 months and 16 years. Concordance between fetuses and infants was substantially greater than that reported in several previous smaller series, with one reporting that a minimally invasive autopsy provided information of at least equivalent clinical significance to that of conventional autopsy in 32 (73%) of 44 fetuses.<sup>7</sup> Post-mortem MRI is particularly valuable for delineation of anatomical abnormalities, and might be better than autopsy for identification of structural brain abnormalities, especially when substantial post-mortem autolysis restricts pathological assessment.<sup>8</sup> The high concordance in fetuses and infants shows the importance of common ancillary studies in this age group.

Conversely, the low concordance in older childhood deaths reflects the different processes that caused those deaths. In children, acquired natural diseases were frequently missed, especially myocarditis, pneumonia, and sepsis. Identification of such diseases usually requires macroscopic and histopathological assessment; specific diagnosis would not be expected from imaging or a blood test. This poorer concordance in children was similar to a large series of adult deaths referred for coroner's autopsy,<sup>9</sup> in which the major discrepancy rate for cause of death

Published Online  
May 16, 2013  
[http://dx.doi.org/10.1016/S0140-6736\(13\)60890-9](http://dx.doi.org/10.1016/S0140-6736(13)60890-9)

See Online/Articles  
[http://dx.doi.org/10.1016/S0140-6736\(13\)60134-8](http://dx.doi.org/10.1016/S0140-6736(13)60134-8)



Patrice Latron/look At Sciences/Science Photo Library

between consensus MRI studies and conventional autopsy was 43% and post-mortem MRI frequently missed common natural disease processes, particularly ischaemic heart disease, pulmonary embolism, pneumonia, intra-abdominal abnormalities, deep venous thrombosis, and malignancy, also confirmed in other studies.<sup>10,11</sup>

Although minimally invasive autopsies have been defined by the UK Human Tissue Act as those in which “needle biopsies through the skin are taken to sample internal organs and tissues, and examinations...[that] use an endoscope or laparoscope to provide internal access to the gastrointestinal tract and the abdominal cavity”;<sup>5</sup> a standard protocol and criteria for adequacy of assessment have not been universally accepted. Identification of when a minimally invasive autopsy is likely to provide an accurate cause of death is crucial to the success of any system of death investigation that uses less invasive techniques. In the present study, predefined criteria were used for a retrospective collaborative review of the minimally invasive autopsies by a pathologist and a radiologist who were masked to the conventional autopsy results. They concluded that a full autopsy might not have been needed in 41% of deaths and, in those cases, there was near-perfect concordance (99.4%) between minimally invasive and conventional autopsy. This assessment resulted in an algorithm that could provide a basis for a collaborative system for death investigation using various diagnostic modalities, both invasive and non-invasive.

The study also confirmed that post-mortem diagnosis of many common diseases presently requires conventional autopsy. As in living patients, histological or cytological assessment is mandatory for specific diagnosis of many neoplastic, infectious, and inflammatory diseases. Histopathological findings might not be uniform; therefore, accurate diagnosis often needs macroscopic assessment of the organs and tissues, and sampling of various sites. Suspicious deaths and other unnatural deaths, including those related to asphyxiation, toxins, or drugs, need complete autopsy to assess natural disease processes accurately and reliably. Multispecialty guidelines to assess possible opiate-related deaths require complete autopsy for possible drug-related deaths, because the toxicological results have to be interpreted in the context of all available information, including autopsy findings.<sup>12</sup> Complex diseases, treatment sequelae, immunosuppression, and

emerging infections will increase the importance of tissue procurement, preservation, and assessment, to assess new therapeutic and disease-prevention strategies.

Despite limitations, Thayyil and colleagues have presented a starting point for development of a robust system for post-mortem diagnosis using various modalities (ie, pathology, radiology, laboratory testing) and a system of interdisciplinary consultation and collaborative diagnosis, mimicking systems for optimum diagnostic assessment of living patients. Some deaths could be assessed with minimally invasive autopsy, but some investigations will mandate use of conventional autopsy. Family members could participate in the decision process. Crucial to success of an integrated post-mortem diagnostic programme will be clear performance standards, regular audits, physician training, and sufficient and stable funding to attract, train, and retain specialists and provide state-of-the-art resources for radiology and pathology. Centres of excellence will provide sufficient resources and interdisciplinary consultation among subspecialty pathologists, radiologists, and clinicians, and will facilitate continued research on translation of multispecialty diagnostic modalities used in living people to the post-mortem setting.

\*Corinne L Fligner, Manjiri K Dighe

Departments of Pathology and Laboratory Medicine, University of Washington, Seattle, WA 98195, USA (CLF); and Department of Radiology, University of Washington Medical Center, Seattle, WA, USA (MKD)

fligner@u.washington.edu

We declare that we have no conflicts of interest.

- 1 Burton EC, Mossa-Basha M. To image or to autopsy? *Ann Intern Med* 2012; **156**: 158–59.
- 2 Shojania KG, Burton EC, McDonald KM, Goldman L. Changes in rates of autopsy-detected diagnostic errors over time: a system review. *JAMA* 2003; **289**: 2849–56.
- 3 Combes A, Mokhtari M, Couvelard A, et al. Clinical and autopsy diagnoses in the intensive care unit: a prospective study. *Arch Intern Med* 2004; **164**: 389–92.
- 4 Gordijn SJ, Erwich JJ, Khong TY. The perinatal autopsy: pertinent issues in multicultural Western Europe. *Eur J Obstet Gynecol Reprod Biol* 2007; **132**: 3–7.
- 5 NMS Implementation Sub-Group of the Department of Health Post Mortem, Forensic and Disaster Imaging Group (PMFDI). Can cross-sectional imaging as an adjunct and/or alternative to the invasive autopsy be implemented within the NHS? October, 2012. <http://www2.le.ac.uk/departments/emfpu/national-documents-1> (accessed Feb 18, 2013).
- 6 Thayyil S, Sebire NE, Chitty LS. Post-mortem MRI versus conventional autopsy in fetuses and children: a prospective validation study. *Lancet* 2013; published online May 16. [http://dx.doi.org/10.1016/S0140-6736\(13\)60134-8](http://dx.doi.org/10.1016/S0140-6736(13)60134-8).
- 7 Breeze AC, Jessop FA, Set PA, et al. Minimally-invasive fetal autopsy using magnetic resonance imaging and percutaneous organ biopsies: clinical value and comparison to conventional autopsy. *Ultrasound Obstet Gynecol* 2011; **37**: 317–23.

- 
- 8 Thayyil S, Chitty LS, Robertson NJ, et al. Minimally invasive fetal postmortem examination using magnetic resonance imaging and computerised tomography: current evidence and practical issues. *Prenat Diagn* 2010; **30**: 713–18.
  - 9 Roberts ISD, Benamore RE, Benbow EW, Lee SH, Harris JN, Jackson A. Post-mortem imaging as an alternative to autopsy in the diagnosis of adult deaths: a validation study. *Lancet* 2012; **379**: 136–42.
  - 10 Wichmann D, Frieder O, Vogel H, et al. Virtual autopsy as an alternative to traditional medical autopsy in the intensive care unit: a prospective cohort study. *Ann Intern Med* 2012; **156**: 123–30.
  - 11 Traill Z. The role of computed tomography and magnetic resonance imaging in the investigation of natural death. *Diagnostic Histopathol* 2010; **16**: 560–64.
  - 12 Davis GG, National Association of Medical Examiners and American College of Medical Toxicology Expert Panel on Evaluating and Reporting Opioid Deaths. Recommendations for the investigation, diagnosis, and certification of deaths related to opioid drugs. *Acad Forensic Pathol* 2013; **3**: 62–76.